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CURRENT OPINION

Ethical Hurdles in the Prioritization of Oncology Care

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Abstract With finite resources, healthcare payers must make difficult choices regarding spending and the ethical distribution of funds. Here, we describe some of the ethical issues surrounding inequity in healthcare in nine major European countries, using cancer care as an example. To identify relevant studies, we conducted a systematic literature search. The results of the literature review suggest that although prevention, access to early diagnosis, and radiotherapy are key factors associated with good outcomes in oncology, public and political attention often focusses on the availability of pharmacological treatments. In some countries this focus may divert funding towards cancer drugs, for example through specific cancer drugs funds, leading to reduced expenditure on other areas of cancer care, including prevention, and potentially on other diseases. In addition, as highly effective, expensive agents are developed, the use of value-based approaches may lead to unacceptable impacts on health budgets, leading to a potential need to re-evaluate current cost-effectiveness thresholds. We anticipate that the question of how to fund new therapies equitably will become even more challenging in the future, with the advent of expensive, innovative, breakthrough treatments in other therapeutic areas.

Key Points for Decision Makers

Cancer survival varies among European countries and is affected by socioeconomic status; prevention, early diagnosis, and radiotherapy are key factors associated with positive outcomes.

Fair reimbursement decisions regarding new expensive drug therapies are a key part of the efforts to improve equity in oncology care spending.

However, political attention can lead to prioritization of funding for certain pharmacological treatments, potentially reducing funding for cancer prevention and the treatment of other diseases.

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1 Introduction

Most European healthcare systems fund medicines through public reimbursement programmes, which aim to facilitate equal access for citizens by eliminating or reducing direct costs to patients. However, regulatory approval of a drug does not guarantee patient access. Reimbursement authorities must assess the benefits of a therapy compared with other available options and establish a fair price, which may be lower than the manufacturer's desired price. Consequently, differences in the approaches, priorities and budgets of different healthcare systems may lead to differences in access to drugs between countries [1–3]. As healthcare is ultimately funded by citizens and healthcare resources are limited, payers must use their budgets sensibly to improve health outcomes in the population for which they are responsible. This can lead to difficult choices regarding spending and the ethical distribution of funds. Although the authors of this article are not ethicists, in April 2015 we met to discuss some of the ethical issues surrounding inequity in healthcare, as they affect payers in the healthcare systems of the nine European countries in which we work. We focussed our discussions on cancer care, a major and increasing component of drug expenditure. Starting from a definition of inequity proposed in 2011—"*Inequity is the presence of systematic and potentially remediable differences among population groups defined socially, economically, or geographically*" [4]—we agreed that therefore, "*health equity is the fair allocation of health determinants and resources in order to maximise health outcomes in all segments of the population, regardless of origin, social background and economic differences*." This definition highlights resource allocation, the aspect of health equity which payers can most readily influence.

Global cancer expenditure has been estimated as US$290 billion (£100 billion on cancer drugs alone in 2014 [5]), and spending is expected to reach US$458 billion by 2030 [6]. In 2009, cancer cost the European Union (EU) €126 billion, with spending in France, Germany, Italy and the UK accounting for two-thirds of the total [7]. With a population increasing in size and age, cancer incidence and the associated costs of treatment are expected to rise worldwide in the coming decades [8–10]. Given the exceptionally emotive nature of cancer, political focus often centres on this therapy area above others, and in particular on the availability of cancer drugs. Recently, the rising cost of cancer treatments has forced many countries to consider mechanisms to contain costs [11], with concerns over potential bottlenecks in the funding of cancer therapies [12]. However, any actions that may place limitations on access to particular therapies are a potential source of inequity.

In this article, we aim to use our real-life experience of European healthcare systems to try to understand some of the causes and consequences of inequity of access to cancer care, with the hope that a common understanding of these issues may aid the development of policies that can reduce inequity. We conducted a literature review to identify relevant publications, with a focus on cancer care as an example (see supplementary material for literature review methods). As well as identifying some of the variation among European countries which may reflect differences in healthcare system funding and organization, we discuss healthcare funding priorities. In particular, we consider the implications of the prioritization of certain interventions through initiatives such as the 2011–2016 Cancer Drugs Fund (CDF) in England.

2 Materials and Methods

To identify studies relevant to the review objectives, a comprehensive, systematic literature search was conducted in Embase, MEDLINE/MEDLINE In-Process, CINAHL, PsycINFO, and the Cochrane Library on 24 December 2014. The search strategy included controlled vocabulary and free text terms, and the search results were filtered using the countries of interest (Supplementary Table 1). The final search results from each database were limited to studies in humans published from 1 January 2009 in English. This time frame was chosen to provide a comprehensive but recent overview of the topic. To supplement the electronic database search, the reference lists of studies identified in a preliminary, non-systematic search were manually screened.

All study types were included with the exception of randomized controlled trials, clinical trials, case reports, case series, case studies, and dissertations. Reviews were included if the focus was on any or all of the countries of interest or reported results for any of the countries of interest. Articles evaluating any type of cancer were included. Articles were included if they examined any type of oncology care (prevention, screening, and treatment) and addressed any of the following objectives: inequality or inequity in access to oncology care in Europe; potential consequences of inequity of access in Europe; ethical issues regarding equity of access to oncology care in Europe. The countries of interest were Belgium, England, France, Germany, Italy, The Netherlands, Scotland, Spain and Sweden. Articles on multiple countries were included if they reported results from any or all of these countries separately. In total, 15 relevant articles were identified (Supplementary Fig. 1; Supplementary Table 2).

3 Results

3.1 Differences in Healthcare and Outcomes Among Countries

Inequity in access to cancer treatment is known to have a measurable impact on patient outcomes [13, 14]. In Europe, the recent EUROCARE studies have investigated differences in cancer treatment and 5-year survival rates across European countries [13, 14]. All-cancer 5-year survival ranged from 37 % in Slovakia to 61 % in Sweden, and correlated linearly with spending ($R = 0.8$; spending was adjusted to take account of the varying purchasing power of national currencies). In general, countries with high spending had high numbers of diagnostic and radiotherapy units, and the number of magnetic resonance imaging (MRI) units per capita directly correlated with survival ($R = 0.7$), reflecting the importance of early diagnosis. Surprisingly, given the political focus on cancer drugs, 5-year survival was more closely linked to the availability of radiotherapy units than to overall healthcare spending, highlighting the importance of efficient resource allocation [13]. A similar analysis used data from the EUROCARE-5 study of 107 cancer registries in Europe to investigate 5-year survival rates for ten common cancers [14]. Countries with high national expenditure on cancer care generally had higher survival rates than those with low expenditure. However, differences among countries with high levels of healthcare spending demonstrated that other factors influence survival rates. Some of these differences may reflect an uneven distribution of different cancer types; for example, the incidence of melanoma in Sweden is approximately three times that in Spain [15]. For patients with similar cancers, comparisons between countries are complicated by a number of factors influencing survival. Explanations for differences in survival between countries may include differences in rates of early diagnosis [16–18], accessibility of medical care other than cancer drugs, different diagnostic intensity and screening approaches, and differences in cancer biology [14]. However, variation in survival may also be a result of differences in socioeconomic status, general health and lifestyle factors (for example, prevalence of smoking) [19].

In addition to the absolute level of expenditure, the organization of care within a healthcare system can improve both efficiency and outcomes. For example, the German certification process for cancer centres is intended to promote collaboration of the various disciplines involved in cancer care, including diagnosis, therapy and aftercare. Such an integrated approach can improve the quality of healthcare processes, as well as treatment satisfaction and outcomes for patients [20]. In addition, there are differences among countries in the availability and funding of cancer screening programmes (for example, Germany is the only country in which skin cancer screening is a standard benefit of public health insurance).

3.2 Differences in Healthcare and Outcomes Within Countries

As well as access at an international level, local socioeconomic and personal factors also influence access to cancer care, and this potential source of inequity is a significant concern for payers within healthcare systems. Across Europe, socioeconomic status, primarily education level and employment status, has been found to have a significant effect on the uptake of cancer screening, even among individuals otherwise using the healthcare system [21–27].

Where screening programmes are available, there is significant variation in the uptake of screening for prostate cancer, breast cancer and cervical cancer [21, 25]. In each case, education levels and/or employment type appear to be significant determinants of screening rates when individuals were required to initiate screening. At a local level, several studies have identified differences in cancer screening rates according to socioeconomic factors, particularly education [22–24, 26, 27]. We note that in addition to taking steps to improve access to screening, it is important for payers to consider which types of cancer screening are beneficial. For example, population-wide prostate cancer screening is associated with only small reductions in mortality, but over-diagnosis and over-treatment are common, and are associated with treatment-related harms [28].

Socioeconomic factors also affect the incidence of particular cancer types and the likely stage at diagnosis [29–32]. In addition, both the speed of treatment initiation and the type of treatment received by patients appear to be negatively influenced by low education and deprivation [33, 34]. For example, a retrospective study in the UK found that patients in affluent areas are more likely to receive treatment for colorectal cancer within 6 months of their first contact with the National Health Service (NHS) than those in deprived areas [34]. Among those receiving treatment, the most deprived patients were less likely to receive treatment within 1 month than the most affluent group, and more likely to receive treatment only after 4–6 months. The most deprived patients were also less likely to survive for 3 years after diagnosis; this difference appears to reflect the delay in treatment initiation [34]. It is possible that patients in the most affluent groups are also likely to be better educated than other groups, and may be more able to seek appropriate and high-quality treatment [34]. The

impact of education level on treatment outcomes has been seen in many studies, including a Swedish analysis that identified significantly higher rates of 5-year colorectal cancer survival for highly educated patients than for those with low education [33]. Similarly, in France a mortality gradient has been described from north to south along the RER B train line which links wealthy central Paris with less affluent suburbs [35].

3.3 Differences in Reimbursement Decision-Making for Medicines in Europe

Health outcomes are also affected by the availability of therapies for patients' specific diseases. Following approval by the European Medicines Agency (EMA), medications that have demonstrated a favourable safety and efficacy profile in evidence-based clinical trials may or may not be granted market access by national health technology assessment (HTA) agencies [1–3]. A recent study evaluated inter-country variability in access by reviewing the number of indications reimbursed by public drug programmes for 10 cancer drugs [3]. Reimbursement varied significantly across Europe, with HTA bodies in England and Scotland recommending for reimbursement fewer than half of 44 indications approved by EMA, mostly owing to a lack of cost effectiveness. However, in several cases in England and Scotland indications that were not initially recommended for reimbursement were subsequently approved with risk-sharing agreements or patient access schemes, or were funded through the CDF [3, 36, 37]. Payers have responsibility for healthcare systems as a whole rather than just oncology, and may sometimes make difficult decisions to limit access to some agents in order to ensure the sustainability of the entire healthcare system. However, in the experience of the authors, payers often take steps to optimize access to effective treatments, even to the extent of overcoming initial negative decisions.

3.4 Healthcare Funding Priorities in Europe

Finite resources mean that governments and payers have to decide on the priorities for their individual healthcare systems. Although access to early diagnosis and radiotherapy are the key factors associated with good outcomes in oncology [13, 16–18], public and political attention often focusses on the availability of cancer drugs [8]. In the EU, cancer drug costs represented 27 % of direct healthcare costs due to cancer in 2009, with considerable variation among countries—in France drug costs were 43 % of the total, compared with 17 % in the Netherlands. This variation may reflect differences in the focus of cancer care spending, although caution is needed when comparing non-drug expenditure due to differences in funding systems and healthcare labour costs [7]. In 2009, Germany spent slightly less than France on cancer drugs, but had double the cancer care budget overall [7], suggesting greater expenditure on other aspects of care, such as access to diagnostic and radiotherapy facilities, which have a significant impact on cancer outcomes [14]. The use of cancer drugs can also vary within a single healthcare system, as shown in a recent analysis in the Netherlands, which found a large variation in the use of particular (expensive) oncology drugs between hospitals [38].

Reimbursement decisions reached through HTA processes [e.g. cost-effectiveness analysis (CEA)] can sometimes be bypassed by alternative mechanisms. For example, from 2011 to 2016 cancer drugs not available through the NHS in England owing to their high cost could be funded by the CDF. However, while the CDF has benefited some patients with cancer, there was a significant level of criticism of this approach, from the National Institute for Health and Care Excellence (NICE) among others [39]. In 2015, an analysis of the costs of a quality-adjusted life-year (QALY) in the healthcare system as a whole suggested that the policy decision to fund expensive therapies through the CDF may have had a detrimental effect on care for patients with non-cancer diseases, and that making the CDF's budget available to the wider NHS would result in much greater improvements in survival and quality of life overall [40]. In response to the financial pressure on the CDF, a new framework was adopted in July 2016 [41]. In this framework, new therapies considered by NICE to be potentially cost effective, but around which there is considerable clinical uncertainly, can be recommended for interim funding through the CDF. The CDF will then operate as a managed access fund, with the level of reimbursement for each therapy agreed between NHS England and the manufacturer, and monitoring of patient and population outcomes. After a data collection period of up to 2 years, each therapy will be reappraised by NICE—it is intended that the reappraisal outcome will be a final positive or negative recommendation.

In addition to the criticism of the 2011–2016 CDF described above, it has been suggested that even when new drugs are deemed cost effective by NICE, the threshold used may be too high [40]. New therapies are typically considered to be cost effective if their incremental cost-effectiveness ratio (ICER), the cost of gaining a fixed improvement in health outcomes compared with existing therapies, is below £30,000 per QALY, with this threshold extended to approximately £50,000 for therapies that can extend life by at least 3 months (typically cancer therapies) [42]. However, NHS expenditure overall was estimated to generate 1 QALY for every £13,000 spent, suggesting that

displacement of existing treatments to fund new, expensive therapies might lead to a net loss of QALYs [40].

These studies raise important issues, and highlight the need for payers to consider the impact of reimbursement for new therapies beyond the patient population in question. The approach taken by NICE in the UK, and by payers across Europe, is more complex than an attempt to maximise QALYs across the healthcare system, and in many cases includes a willingness to encourage the development of innovative new medicines and devices [43]. However, while all payers aim to provide patients with access to the most effective treatments, ultimately with curative intent, it is also important that funding can be provided for other aspects of cancer care, including screening, early diagnosis, radiotherapy and palliative care. At a national level, individual countries' cancer plans take into account all aspects of care. However, it is possible that initiatives such as the 2011–2016 CDF may divert funding towards cancer drugs, leading to reduced expenditure on early diagnosis and radiotherapy, and thereby potentially doing harm to care outcomes overall. As well as allocating resources appropriately within cancer care, payers must also ensure that other disease areas are treated fairly, both in terms of managing major costs to the healthcare system in other areas and of avoiding cuts to budgets in areas that may be less costly and less high profile than oncology, but represent good value for money [40].

In some countries, for example Germany, the healthcare system does not give priority to particular disease areas. However, funding arrangements such as the CDF exist in a number of other countries, demonstrating a political willingness to overturn technical decisions on reimbursement. For example, the Italian government has established a fund to reimburse the costs of new innovative medicines, as well as a separate fund for new hepatitis C drugs, although with restrictions on the number of patients to be treated. A fund for new hepatitis C treatments has also been set up in the UK. A number of therapies for orphan diseases have also been made available through special earmarked funds. In each case, funding of one disease area over another is potentially problematic—in the UK at least this may undermine the fundamental NHS principle that all patients should be treated equitably. If funding is to be allocated according to the priority assigned to different disease areas, this raises a fundamental problem: how does one decide whether it is worse to have cancer than another disease such as heart failure? In systems that make use of the QALY in order to compare health outcomes across different disease areas ("a QALY is a QALY is a QALY") [44] it is not obvious that there should be a willingness to pay more for a QALY in one disease area than in another.

It is theoretically possible that in a particular country, society as a whole may decide that increased funding should be given to cancer therapies, even at the expense of other disease areas. If this is the case, rather than overriding the decision-making processes of HTA bodies, it may be more effective to capture such societal preferences through evaluation approaches such as value-based assessment. In principle, such processes could allow prioritization of the use of healthcare budgets without leading to inequity of access from the perspective of society. More general attempts have also been made to take the views of patients and of society as a whole into account in reimbursement decision making. In the Netherlands, the National Healthcare Institute has recently announced that willingness-to-pay levels for new therapies will be weighted according to disease burden [45]. In Belgium, a recent "citizens' lab" initiative has revealed that society seems to favour quality of life and longer-term benefits as major criteria for reimbursement of novel therapeutics [46]. In addition, the Scottish Medicines Consortium, will accept more uncertainty in the economic case for medicines licensed for the treatment of orphan diseases, and will accept a higher ICER for treatments providing a substantial improvement in life expectancy [47]. NICE also consider life extension at the end of life, as well as innovation and the non-health objectives of the NHS [48]. Recently, further proposed 'modifiers'—including burden of illness and wider societal impact have been investigated in public preference surveys [49–51]. Although proposals to prioritize innovative treatments and those for severe diseases were broadly supported [49, 51], results were inconsistent with regard to an end-of-life premium [49–51]. Participants in one study reported a substantial preference for health-related quality of life improvement over life extension [50]—in oncology, this may suggest that greater attention should be paid to the side-effect profiles of therapies, and to the role of palliative care.

3.5 Legal Implications of Healthcare Decision-Making

Ultimately, the consequence of any system of decision making in healthcare is that some therapies may not be made available to patients. In addition to the need to avoid possible inequity, the legal system in each country must be considered. In the UK, access to a drug cannot be rejected absolutely for any reason other than safety. Although it would in most cases be politically and ethically difficult to justify, rationing based on evidence and within equality legislation is not illegal [52]. In Sweden, rationing is allowed in the context of prioritization, provided allocation of treatment is done in a transparent manner [53]. In Belgium the legal system does not cover rationing. The Spanish Constitution is ambiguous: rationing beyond national processes is possible through regional

reimbursement decisions, but is unlikely to be supported by the courts, which cannot back restrictions on a publicly available drug. In France, reducing social inequalities for those affected by cancer is the main goal of the 2014–2019 national cancer plan [54]. The influence of these differences is not straightforward, and in some cases there may be potential for legal challenges to decisions made in the interests of equitable distribution of healthcare resources.

3.6 Sustainability of Healthcare Funding

Much debate focusses on the possibility of funding expensive treatments. However, from a payer perspective it is at least as important to consider whether the price levels that force payers and politicians into the current discussions and conflicts are sustainable. Overall, drug expenditure has risen significantly in recent years, and in countries such as Germany has almost doubled since the beginning of the century. Particularly in oncology, with new treatment options and combination therapies available in the near future, it is likely that the response from healthcare systems will not be limited to attempts to prioritize or to increase budgets. In addition, we may expect in the future to see an introduction of some pricing elements based on development and manufacturing costs. Pricing using a purely value-based approach may lead to therapies being deemed cost effective under current thresholds, but having an ultimately unaffordable impact on healthcare budgets. CEA (which is less central to decision making in European countries such as France and Germany than in the UK and Sweden) is therefore only part of the solution to funding costly medicines. Where CEA is a major factor in decision making, it has been suggested that lower cost-effectiveness thresholds may be needed for therapies with a very large budget impact [40].

4 Discussion

Cancer is a leading cause of death and morbidity throughout the world, and an increasing component of total healthcare spending. Consideration of the cost of cancer care raises questions regarding how healthcare payers balance access, quality, equity and cost. Essentially, all countries must ration healthcare to some extent, but questions exist around how this should be accomplished, and whether there is political and public agreement with the chosen approach. As a result, there are substantial differences in healthcare and outcomes between European countries. Many of these differences represent substantial equity issues that cannot readily be addressed by healthcare payers and decision makers within a specific country. However, differences between countries can provide insights that can be used to improve healthcare within an individual system. Indeed, inequity within countries—differences in treatment and outcomes that are related to socioeconomic or geographical factors—remains a serious concern in Europe. It is possible to address some of the sources of inequity through organizational approaches, such as a national cancer plan, designated cancer centres, routine provision of second opinions and the integration of care to provide patients with a single point of contact. Educational measures aimed at improving health literacy are also likely to be beneficial, particularly in improving early diagnosis and treatment. Fair reimbursement decisions regarding new expensive drug therapies are also a key part of the efforts to reach better equity in oncology care spending.

Reimbursement decisions should be taken with the aim of making effective therapies available to patients while avoiding an inequitable distribution of resources. In a healthcare system with a finite budget, this may mean that in some cases negative decisions are appropriate. By contrast, prioritization of certain disease areas, particularly cancer, through political initiatives may have unintended consequences for the healthcare system as a whole. By ring-fencing funds for one aspect of healthcare, other, potentially more cost-effective areas may have their budgets reduced. More widely, funding drug therapies in a fair way is challenging, with effective, innovative agents often associated with high costs. There is some evidence that society as a whole may support prioritization of therapies in certain areas, particularly cancer. As members of society are ultimately the funders of our healthcare systems, it may be that a higher willingness to pay is appropriate in some disease areas—this is the subject of ongoing research in a number of countries. It is therefore likely that price structures and valuation models may change in the future. For example, payers have suggested innovative pricing strategies for gene therapies which may lead to price levels that are more sustainable in the long term [55]. The question of how to fund new therapies equitably is a major issue at present, and is likely to become even more challenging in the future, with the advent of expensive, innovative, breakthrough treatments.

This review has some limitations. In particular, equity in oncology care is affected by a number of factors, and the rapidly evolving systems and processes across Europe makes the identification of the causes of inequity challenging. However, the authors as a group have noted differences in equity among the countries in which we work, and believe that our real-life experience has allowed us to identify some of the key issues in oncology funding, with the goal of furthering a common understanding of equity in healthcare.

In conclusion, the findings of this review suggest that there is a high degree of awareness of inequity in cancer care in Europe. Payers attempt to allocate budgets fairly, while following the preferences of patients and society where possible. Given budget constraints, however, decisions on spending and drug reimbursement inevitably affect equity, either directly by limiting access to a particular treatment, or indirectly by reducing the funding available in other areas. Several different methods are used in European countries to justify funding decisions, based on a number of criteria. Future research is needed to advance our understanding of the complexity of the causes of differences in outcomes, and to help develop new policies aimed at reducing inequity.

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Compliance with Ethical Standards

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